

AMENDMENTS TO THE SPECIFICATION

Please replace paragraph [0010] with the following paragraph:

[0010] In addition to clomiphene, women have been treated with ovulation induction regimens which include commercial preparations of the human gonadotropins, including follicle stimulating hormone (FSH) and luteinizing hormone (LH) or chorionic gonadotropin (CG), all of which were first obtained by purification of urine from pregnant women and more recently by recombinant technology. In general, this treatment is highly effective in stimulating folliculogenesis and steroidogenesis. Complications of this treatment result from the fact that these preparations and regimens can over-stimulate follicular development and maturation of follicles. In a subset of patients, the ovary can become hyperstimulated, which may result in multiple ovulations and, consequently, multiple births. Not only can ovarian hyperstimulation be life threatening to the mother, it also typically results in newborns with lower birth weight, who subsequently require intensive care. It is believed that the principal complications attributed to gonadotropin-induced hyperstimulation and multiple pregnancies probably result from the prolonged effects of human chorionic gonadotropin (hCH) hCG. In addition, use of gonadotropins in ovulation induction regimens can result in injection site reactions, both local and systemic. Consequently, the development of ovulation induction regimens using orally active agents with milder gonadotropin-like activity as opposed to therapies that use potent injectables would be of substantial benefit. More importantly, it would be a significant advantage if ovulation induction regimens could be developed which result in less ovarian hyperstimulation and, consequently, present less danger to the mother and produce healthier newborns.

Please replace paragraph [0011] with the following paragraph:

[0011] In a first aspect, the invention provides a use of a non-peptide cAMP level modulator, preferably a phosphodiesterase (PDE) PDE inhibitor, more preferably a PDE4 inhibitor, for the manufacture of a medicament for the induction of ovulation in a patient.

Please replace paragraph [0112] with the following paragraph:

[0112] Ovaries were removed from immature 25 day old, hypophysectomized, diethylstilbesterol treated Sprague-Dawley rats. The ovaries were repeatedly punctured with 27 gauge needles to liberate granulosa cells from the follicles. Cells were washed and re-suspended in McCoys 5A media + 0.1% BSA + 2 µM

androstenedione. Viable cells in number of 100,000 were loaded into 6-well tissue culture dishes in a 1.0 ml volume (with Compound 1 and Compound 2 at a concentration of 25 micromolar, either alone or in conjunction with a low, 0.1 pM dose of gonadotropin). Plates were incubated in a 37°C incubator, 100% humidity, 5.0% CO₂ for 48 hrs. Conditioned media were assayed in a cAMP specific radioimmunoassay (RIA) ~~RIA~~. Results are expressed as mean plus or minus standard deviations. As seen in Figure 2, Compounds 1 and 2 cause a significant increase in cAMP levels in the presence of sub-effective concentrations of gonadotropin.